

| L Number | Hits | Search Text  | DB  | Time stamp       |
|----------|------|--|---|------------------|
| 33       | 49   | Receptor ADJ advanced ADJ glycation  | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 14:47 |
| 40       | 5    | (US-20020002203-\$ or US-20010053357-\$ or US-20010039256-\$).did. or (WO-9918987-\$).did. or (US-20010039256-\$ or WO-200020458-\$ or WO-200020621-\$ or WO-9954485-\$ or US-20010053357-\$).did.   | US-PGPUB;<br>EPO;<br>DERWENT                          | 2003/03/27 14:45 |
| 49       | 4    | (Receptor ADJ advanced ADJ glycation) SAME amphoterin  | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 14:53 |
| 56       | 15   | Morser ADJ Michael ADJ John  | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 14:54 |
| 63       | 29   | (US-6465422-\$ or US-5864018-\$ or US-5811401-\$).did. or (US-20010039256-\$ or US-20020002203-\$ or US-20010053357-\$ or US-20030059423-\$ or US-20030037344-\$ or US-20030032663-\$ or US-20020177550-\$ or US-20020122799-\$ or US-20020116725-\$ or US-20020106726-\$ or US-20020013256-\$ or US-20010041349-\$).did. or (WO-9918987-\$ or WO-9954485-\$ or WO-9907402-\$ or WO-9822138-\$ or WO-9726913-\$ or WO-9739121-\$).did. or (WO-200020621-\$ or WO-200020458-\$ or WO-200274805-\$ or WO-200230889-\$ or US-20020116725-\$ or US-20020106726-\$ or US-6465422-\$ or US-20010039256-\$ or US-20010053357-\$).did. | USPAT;<br>US-PGPUB;<br>EPO;<br>DERWENT                | 2003/03/27 14:56 |
| -        | 18   | (Receptor SAME (advanced ADJ glycation) ) and RAGE   | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2002/05/16 10:39 |
| -        | 42   | RAGE and (advanced ADJ glycation)  | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 14:15 |
| -        | 34   | (Receptor SAME (advanced ADJ glycation) ) and (cancer or tumor or mata\$10 or neoplas\$5)  | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 14:27 |
| -        | 77   | Receptor SAME (advanced ADJ glycation)   | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 14:45 |

| L Number | Hits | Search Text  | DB  | Time stamp       |
|----------|------|--|---|------------------|
| 13       | 87   | Receptor SAME advanced SAME glycation  | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 16:18 |
| 20       | 0    | (Receptor SAME advanced SAME glycation ) and (extracelular SAME matri\$5)  | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 16:19 |
| 27       | 26   | (Receptor SAME advanced SAME glycation ) and (laminin fibronectin amphoterin caderin integrin hyaluronic integrin amphoterin)  | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 16:26 |
| 34       | 104  | RAGE and (laminin fibronectin amphoterin caderin integrin hyaluronic integrin amphoterin)  | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 16:26 |
| -        | 18   | (Receptor SAME (advanced ADJ glycation) ) and RAGE   | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2002/05/16 10:39 |
| -        | 42   | RAGE and (advanced ADJ glycation)  | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 14:15 |
| -        | 34   | (Receptor SAME (advanced ADJ glycation) ) and (cancer or tumor or mata\$10 or neoplas\$5)  | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 14:27 |
| -        | 77   | Receptor SAME (advanced ADJ glycation)   | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 16:17 |
| -        | 49   | Receptor ADJ advanced ADJ glycation  | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 14:47 |
| -        | 5    | (US-20020002203-\$ or US-20010053357-\$ or US-20010039256-\$).did. or (WO-9918987-\$).did. or (US-20010039256-\$ or WO-200020458-\$ or WO-200020621-\$ or WO-9954485-\$ or US-20010053357-\$).did. | US-PGPUB;<br>EPO;<br>DERWENT                          | 2003/03/27 14:45 |
| -        | 4    | (Receptor ADJ advanced ADJ glycation)SAME amphoterin   | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 14:53 |
| -        | 15   | Morser ADJ Michael ADJ John  | USPAT;<br>US-PGPUB;<br>EPO; JPO;<br>DERWENT;<br>USOCR | 2003/03/27 14:54 |

|   |    |  |  |                  |
|---|----|--|--|------------------|
| - | 29 | (US-6465422-\$ or US-5864018-\$ or<br>US-5811401-\$).did. or (US-20010039256-\$ or<br>US-20020002203-\$ or US-20010053357-\$ or<br>US-20030059423-\$ or US-20030037344-\$ or<br>US-20030032663-\$ or US-20020177550-\$ or<br>US-20020122799-\$ or US-20020116725-\$ or<br>US-20020106726-\$ or US-20020013256-\$ or<br>US-20010041349-\$).did. or (WO-9918987-\$ or<br>WO-9954485-\$ or WO-9907402-\$ or<br>WO-9822138-\$ or WO-9726913-\$ or<br>WO-9739121-\$).did. or (WO-200020621-\$ or<br>WO-200020458-\$ or WO-200274805-\$ or<br>WO-200230889-\$ or US-20020116725-\$ or<br>US-20020106726-\$ or US-6465422-\$ or<br>US-20010039256-\$ or US-20010053357-\$).did. | USPAT;<br>US-PGPUB;<br>EPO;<br>DERWENT | 2003/03/27 14:56 |
|---|----|--|--|------------------|

(FILE 'HOME' ENTERED AT 16:40:54 ON 27 MAR 2003)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICNF' ENTERED  
AT 16:41:02 ON 27 MAR 2003

L1 3464 S (RECEPTOR FOR ADVANCED GLYCATION ENDPRODUCT?) OR RAGE  
L2 137 S L1 AND (LAMININ OR FIBRONECTIN OR AMPHOTERIN OR CADERIN OR IN  
L3 64 DUP REM L2 (73 DUPLICATES REMOVED)  
L4 64 FOCUS L3 1-  
L5 14 S L4 AND PY<=1998  
L6 14 SORT L5 PY

=> d an ti so au ab pi l6 5 6 10 14

L6 ANSWER 5 OF 14 MEDLINE

AN 96029671 MEDLINE

TI The receptor for advanced glycation end products (**RAGE**) is a cellular binding site for **amphoterin**. Mediation of neurite outgrowth and co-expression of **rage** and **amphoterin** in the developing nervous system.

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Oct 27) 270 (43) 25752-61.

Journal code: 2985121R. ISSN: 0021-9258.

AU Hori O; Brett J; Slattery T; Cao R; Zhang J; Chen J X; Nagashima M; Lundh E R; Vijay S; Nitecki D; +

AB The receptor for advanced glycation end products (**RAGE**), a newly-identified member of the immunoglobulin superfamily, mediates interactions of advanced glycation end product (AGE)-modified proteins with endothelium and other cell types. Survey of normal tissues demonstrated **RAGE** expression in situations in which accumulation of AGEs would be unexpected, leading to the hypothesis that under physiologic circumstances, **RAGE** might mediate interaction with ligands distinct from AGEs. Sequential chromatography of bovine lung extract identified polypeptides with M(r) values of approximately 12,000 (p12) and approximately 23,000 (p23) which bound **RAGE**. NH2-terminal and internal protein sequence data for p23 matched that reported previously for **amphoterin**. **Amphoterin** purified from rat brain or recombinant rat **amphoterin** bound to purified sRAGE in a saturable and dose-dependent manner, blocked by anti-**RAGE** IgG or a soluble form of **RAGE** (sRAGE). Cultured embryonic rat neurons, which express **RAGE**, displayed dose-dependent binding of 125I-**amphoterin** which was prevented by blockade of **RAGE** using antibody to the receptor or excess soluble receptor (sRAGE). A functional correlate of **RAGE-amphoterin** interaction was inhibition by anti-**RAGE** F(ab')2 and sRAGE of neurite formation by cortical neurons specifically on **amphoterin**-coated substrates. Consistent with a potential role for **RAGE-amphoterin** interaction in development, **amphoterin** and **RAGE** mRNA/antigen were co-localized in developing rat brain. These data indicate that **RAGE** has physiologically relevant ligands distinct from AGEs which are likely, via their interaction with the receptor, to participate in physiologic processes outside of the context of diabetes and accumulation of AGEs.

L6 ANSWER 6 OF 14 SCISEARCH COPYRIGHT 2003 ISI (R)

AN 95:201535 SCISEARCH

TI THE RECEPTOR FOR ADVANCED GLYCATION ENDPRODUCTS (**RAGE**) IS A CELL-SURFACE RECEPTOR FOR **AMPHOTERIN** IN THE DEVELOPING CENTRAL-NERVOUS-SYSTEM (CNS) TO PROMOTE NEURITE OUTGROWTH

SO FASEB JOURNAL, (09 MAR 1995) Vol. 9, No. 3, Part 1, pp. A382. ISSN: 0892-6638.

AU HORI O (Reprint); CAO R; BRETT J; SLATTERY T; NAGASHIMA M; NITECKI D; MORSE J; STERN D; SCHMIDT A M

L6 ANSWER 10 OF 14 MEDLINE

AN 1999030344 MEDLINE

TI Spl-binding elements in the promoter of **RAGE** are essential for **amphoterin**-mediated gene expression in cultured neuroblastoma cells.

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Nov 20) 273 (47) 30870-8. Journal code: 2985121R. ISSN: 0021-9258.

AU Li J; Qu X; Schmidt A M  
 AB Receptor for AGE (**RAGE**) and the polypeptide **amphoterin** are highly expressed and co-localized in neurons of the developing central nervous system of the rat. In vitro, the interaction of **amphoterin** with neuronal **RAGE** induces neurite outgrowth. We tested the hypothesis that interaction of **amphoterin** with neuronal cells enhances **RAGE** expression, thereby providing a mechanism by which **amphoterin**-mediated regulation of **RAGE** might contribute to promotion of neurite growth and spreading. Incubation of cultured neuroblastoma cells with **amphoterin** resulted in increased transcription and translation of **RAGE**, a process largely inhibited in the presence of anti-**RAGE** IgG but not by nonimmune IgG. To begin to delineate molecular mechanisms underlying these findings, we identified multiple putative binding elements within the 5'-flanking region of the **RAGE** gene for Sp1, a transcription factor that has been critically linked to the process of normal development. DNase I footprinting and electrophoretic mobility shift assays demonstrated multiple functional Sp1-binding sites within the region -245 to -40 of the **RAGE** promoter. Transient transfection of cultured SK-N-SH neuroblastoma cells with chimeric 5'-deletion constructs linked to luciferase reporter revealed that the region containing Sp1-binding elements did not contribute uniquely to basal expression of the **RAGE** gene. Simultaneous mutation of the multiple Sp1-binding elements in this region did not affect basal promoter function; however, promoter responsiveness to **amphoterin** was markedly attenuated. These results point to Sp1-dependent mechanisms underlying **amphoterin**-mediated increases in **RAGE** expression in neuroblastoma cells and further link **amphoterin-RAGE** interaction to development of the nervous system.

L6 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2003 ACS

AN 1997:719241 CAPLUS

DN 128:2367

TI **RAGE**: a receptor with a taste for multiple ligands and varied pathophysiologic states

SO Hormones and Signaling (1998), 1, 41-63

CODEN: HOSIFO

AU Schmidt, Ann Marie; Wautier, Jean-Luc; Stern, David; Yan, Shi Du  
 AB A review with 35 refs. The classical concept of one receptor with specificity and high affinity for only one ligand has evolved considerably. Furthermore, there are apparently accidental but, nonetheless, pathophysiologic relevant ligands, such as intercellular adhesion mol.-1, which interacts with rhinoviruses to facilitate their entry into cells. **RAGE**, a member of the Ig of cell surface mols., shares such properties. **RAGE** interacts with different ligands, with varied implications for cellular functions, depending on the physiologic or pathophysiologic setting. For example, during normal development, **RAGE** interacts with **amphoterin**, a mol. which promotes neurite out-growth. In pathophysiologic states such as diabetes or amyloidosis obsd. in the setting of renal dialysis, **RAGE** binds non-enzymically glycosylated adducts of macromols. termed Advanced Glycation Endproducts, or AGEs, resulting in perturbation of multiple cellular properties. Alzheimer's disease represents a situation in which **RAGE** expression increases dramatically, and amyloid-beta peptide, thought to be crit. to the pathogenesis of neurodegeneration, is another ligand for **RAGE**. The diverse circumstances in which these varied ligands interact with **RAGE** are the subject of intense investigation to understand the distinct mechanisms that regulate the temporal and spatial expression of this receptor.

=>

L4 ANSWER 1 OF 64 CAPLUS COPYRIGHT 2003 ACS  
 AN 1999:691229 CAPLUS  
 DN 131:317761  
 TI Inhibition of tumor invasion or spreading based on a soluble receptor for advanced glycation endproducts  
 SO PCT Int. Appl., 88 pp.  
 CODEN: PIXXD2  
 IN Schmidt, Ann Marie; Stern, David  
 AB The present invention provides for a method for inhibiting tumor invasion or metastasis in a subject which comprises administering to the subject a therapeutically effective amt. of a form of sol. receptor for advanced glycation endproducts (**RAGE**). Interruption of cellular **RAGE**-extracellular matrix (**amphoterin** and/or similar structures) interaction appears to be at least one mechanism by which **sRAGE** limits tumor growth. The present invention also provides a method for evaluating the ability of an agent to inhibit tumor invasion in a local cellular environment which comprises: (a) admixing with cell culture media an effective amt. of the agent; (b) contacting a tumor cell in cell culture with the media from step (a); (c) detg. the amt. of spreading of the tumor cell culture, and (d) comparing the amt. of spreading of the tumor cell culture detd. in step (c) with the amt. detd. in the absence of the agent, thus evaluating the ability of the agent to inhibit tumor invasion in the local cellular environment. The present invention also provides a pharmaceutical compn. which comprises a therapeutically effective amt. of the agent evaluated in the aforementioned method and a pharmaceutically acceptable carrier.

| PATENT NO.    | KIND   | DATE     | APPLICATION NO. | DATE     |
|---------------|--|----------|-----------------|----------|
| WO 9954485    | A1   | 19991028 | WO 1999-US8427  | 19990416 |
| W:            | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
| RW:           | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |          |                 |          |
| US 6465422    | B1   | 20021015 | US 1998-62365   | 19980417 |
| CA 2325573    | AA   | 19991028 | CA 1999-2325573 | 19990416 |
| AU 9934957    | A1   | 19991108 | AU 1999-34957   | 19990416 |
| EP 1071794    | A1   | 20010131 | EP 1999-916699  | 19990416 |
| R:            | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI   |          |                 |          |
| JP 2002512038 | T2   | 20020423 | JP 2000-544814  | 19990416 |
| US 2002177550 | A1   | 20021128 | US 2001-851071  | 20010508 |

L4 ANSWER 2 OF 64 MEDLINE  
 AN 96029671 MEDLINE  
 TI The receptor for advanced glycation end products (**RAGE**) is a cellular binding site for **amphoterin**. Mediation of neurite outgrowth and co-expression of **rage** and **amphoterin** in the developing nervous system.  
 SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Oct 27) 270 (43) 25752-61. Journal code: 2985121R. ISSN: 0021-9258.  
 AU Hori O; Brett J; Slaterry T; Cao R; Zhang J; Chen J X; Nagashima M; Lundh E R; Vijay S; Nitecki D; +  
 AB The receptor for advanced glycation end products (**RAGE**), a newly-identified member of the immunoglobulin superfamily, mediates interactions of advanced glycation end product (AGE)-modified proteins with endothelium and other cell types. Survey of normal tissues demonstrated **RAGE** expression in situations in which accumulation of AGEs would be unexpected, leading to the hypothesis that under physiologic circumstances, **RAGE** might mediate interaction with ligands distinct from AGEs. Sequential chromatography of bovine lung extract identified polypeptides with M(r) values of approximately 12,000 (p12) and approximately 23,000 (p23) which bound **RAGE**. NH2-terminal and internal protein sequence data for p23 matched that reported previously for **amphoterin**. **Amphoterin**

purified from rat brain or recombinant rat **amphoterin** bound to purified sRAGE in a saturable and dose-dependent manner, blocked by anti-**RAGE** IgG or a soluble form of **RAGE** (sRAGE). Cultured embryonic rat neurons, which express **RAGE**, displayed dose-dependent binding of <sup>125</sup>I-**amphoterin** which was prevented by blockade of **RAGE** using antibody to the receptor or excess soluble receptor (sRAGE). A functional correlate of **RAGE-amphoterin** interaction was inhibition by anti-**RAGE** F(ab')<sub>2</sub> and sRAGE of neurite formation by cortical neurons specifically on **amphoterin**-coated substrates. Consistent with a potential role for **RAGE-amphoterin** interaction in development, **amphoterin** and **RAGE** mRNA/antigen were co-localized in developing rat brain. These data indicate that **RAGE** has physiologically relevant ligands distinct from AGEs which are likely, via their interaction with the receptor, to participate in physiologic processes outside of the context of diabetes and accumulation of AGEs.

- L4 ANSWER 3 OF 64 MEDLINE  
 AN 2003125715 IN-PROCESS  
 TI Differential effects between **amphoterin** and advanced glycation end products on colon cancer cells.  
 SO INTERNATIONAL JOURNAL OF CANCER, (2003 May 10) 104 (6) 722-7. Journal code: 0042124. ISSN: 0020-7136.  
 AU Kuniyasu Hiroki; Chihara Yoshitomo; Kondo Hideaki  
 AB **Amphoterin** is 1 ligand of the receptor for advanced glycation end products (**RAGE**). We studied expression of **amphoterin** and **RAGE** mRNA and proteins in colorectal carcinoma cells and investigated their associations with the invasive activities of cells exposed to advanced glycation end products (AGE). Expression of **RAGE** and **amphoterin** was examined in 4 colorectal carcinoma cell lines. All cell lines expressed both **RAGE** and **amphoterin**. The effects of **RAGE** and **amphoterin** on cell growth (MTT assay), migration (wound healing assay) and invasion (in vitro invasion assay) were tested by treatment of cells with **RAGE** and **amphoterin** antisense S-oligodeoxynucleotides (ODNs). Cell growth, migration and invasion were inhibited significantly in Colo320 and WiDr carcinoma cells treated with **RAGE** and **amphoterin** antisense S-ODNs compared with sense-treated cells. Differences in ligand activity between **amphoterin** and AGE were examined with AGE-bovine serum albumin (BSA). AGE-BSA decreased cell growth, migration and invasion of **amphoterin** antisense S-ODN-treated Colo320 and WiDr cells compared with those of cells treated with Colo320 conditioned medium. Phosphorylation of extracellular signal-regulated kinase-1/2, Rac1 and AKT and production of matrix metalloproteinase 9 were increased to a greater degree by **amphoterin** than by AGE-BSA. In contrast, production of inducible nitric oxide synthase and nuclear factor-kappaBp65 were increased to a greater degree by AGE-BSA than by **amphoterin**.  
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- L4 ANSWER 4 OF 64 CAPLUS COPYRIGHT 2003 ACS  
 AN 2002:695779 CAPLUS  
 DN 137:232649  
 TI Benzimidazole derivatives as therapeutic agents  
 SO PCT Int. Appl., 61 pp. CODEN: PIXXD2  
 IN Mjalli, Adnan M. M.; Gopalaswamy, Ramesh  
 AB Benzimidazole derivs. having arom. groups at the 2-position, optionally sepd. from the imidazole ring by substituted alkane chain such as I are manufd. and are useful as modulators of the interaction between the receptor for advanced glycated end products (**RAGE**) and its ligands, such as advanced glycated end products (AGEs), S100/calgranulin/EN-**RAGE**, .beta.-amyloid and **amphoterin**, and for the management, treatment, control, or as an adjunct treatment for diseases in humans caused by **RAGE**. Such diseases or disease states include acute and chronic inflammation, the development of diabetic late complications such as increased vascular permeability, nephropathy, atherosclerosis, and retinopathy, the development of Alzheimer's disease, erectile dysfunction, and tumor invasion and metastasis. I was manufd. by reaction of BOC-D-(O-benzyl)tyrosine with iso-Bu chloroformate and

N,O-dimethylhydroxylamine hydrochloride at -15.degree. to room temp., redn. of the resulting amide with LiAlH<sub>4</sub>, and reaction of the resulting amino aldehyde overnight in EtOH with a diaminophenol prepd. by reaction of 3-fluoro-4-nitrophenol with BuNH<sub>2</sub> and redn. of the resulting 3-butylamino-4-nitrophenol with SnCl<sub>2</sub>.2H<sub>2</sub>O.

|    | PATENT NO.    | KIND   | DATE     | APPLICATION NO. | DATE     |
|----|---------------|--|----------|-----------------|----------|
| PI | WO 2002069965 | A1   | 20020912 | WO 2002-US6706  | 20020305 |
|    | W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
|    | RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |          |
|    | US 2003032663 | A1   | 20030213 | US 2002-91609   | 20020305 |

L4 ANSWER 5 OF 64 CAPLUS COPYRIGHT 2003 ACS

AN 2002:695943 CAPLUS

DN 137:216780

TI Preparation of aromatic carboxamides as modulators of receptor for advanced glycated end products (**RAGE**).

SO PCT Int. Appl., 95 pp.

CODEN: PIXXD2

IN Mjalli, Adnan M. M.; Andrews, Rob; Wysong, Christopher

AB G2R1R2CG1CONR3R4 [I; G1 = alkylene; G2 = H, alkyl, aryl, alkylaryl, amino, (substituted) imidazolyl; R1 = H, alkyl, aryl, alkylaryl; R2 = alkyl, aryl, aralkyl, etc.; R3 = H, alkyl, alkylaryl, alkoxyaryl; R4 = alkylaryl, alkoxyaryl, aryl], were prepd. I are modulators of the interaction between the receptor for advanced glycated end products (**RAGE**) and its ligands, such as advanced glycated end products (AGEs), S100/calgranulin/EN-**RAGE**, .beta.-amyloid and **amphoterin**. I are useful in treating inflammation, the development of diabetic late complications such as increased vascular permeability, nephropathy, atherosclerosis, and retinopathy, the development of Alzheimer's disease, erectile dysfunction, and tumor invasion and metastasis. Thus, 3-(3-tert-butoxyphenyl)-3-(9-fluorenylmethoxycarbonylamino)propionic acid, HTBU, diisopropylethylamine, and 2,4-bis-(3-diethylaminopropoxy)aniline (prepn. given) were stirred overnight in MeCN to give 3-(3-tert-butoxyphenyl)-3-(9-fluorenylmethoxycarbonylamino)propionic acid 2,4-bis-(3-diethylaminopropoxy)aniline amide. The latter showed IC<sub>50</sub><0.5 .mu.M for inhibition of binding of **RAGE** to s100b.

|    | PATENT NO.    | KIND   | DATE     | APPLICATION NO. | DATE     |
|----|---------------|--|----------|-----------------|----------|
| PI | WO 2002070473 | A2   | 20020912 | WO 2002-US6707  | 20020305 |
|    | WO 2002070473 | A3   | 20021227 |                 |          |
|    | W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
|    | RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |          |
|    | US 2002193432 | A1   | 20021219 | US 2002-91759   | 20020305 |

L4 ANSWER 6 OF 64 CAPLUS COPYRIGHT 2003 ACS

AN 1997:719241 CAPLUS

DN 128:2367

TI **RAGE**: a receptor with a taste for multiple ligands and varied pathophysiologic states

SO Hormones and Signaling (1998), 1, 41-63

CODEN: HOSIFO

AU Schmidt, Ann Marie; Wautier, Jean-Luc; Stern, David; Yan, Shi Du

AB A review with 35 refs. The classical concept of one receptor with



specificity and high affinity for only one ligand has evolved considerably. Furthermore, there are apparently accidental but, nonetheless, pathophysiol. relevant ligands, such as intercellular adhesion mol.-1, which interacts with rhinoviruses to facilitate their entry into cells. **RAGE**, a member of the Ig of cell surface mols., shares such properties. **RAGE** interacts with different ligands, with varied implications for cellular functions, depending on the physiol. or pathophysiol. setting. For example, during normal development, **RAGE** interacts with **amphoterin**, a mol. which promotes neurite out-growth. In pathophysiol. states such as diabetes or amyloidosis obsd. in the setting of renal dialysis, **RAGE** binds non-enzymically glycated adducts of macromols. termed Advanced Glycation Endproducts, or AGEs, resulting in perturbation of multiple cellular properties. Alzheimer's disease represents a situation in which **RAGE** expression increases dramatically, and amyloid-beta peptide, thought to be crit. to the pathogenesis of neurodegeneration, is another ligand for **RAGE**. The diverse circumstances in which these varied ligands interact with **RAGE** are the subject of intense investigation to understand the distinct mechanisms that regulate the temporal and spatial expression of this receptor.

L4 ANSWER 7 OF 64 CAPLUS COPYRIGHT 2003 ACS

AN 2002:416565 CAPLUS

DN 136:383855

TI Effect of receptor for advanced glycation endproducts (**RAGE**) on invasion and metastasis of human pancreatic carcinoma cell

SO Nagoya-shiritsu Daigaku Igakkai Zasshi (2002), 53(1), 143-149

CODEN: NASDA6; ISSN: 0027-7606

AU Ohara, Eiko

AB Receptor for advanced glycation endproducts (**RAGE**) was expressed at mRNA and protein levels in human pancreatic cancer cell lines, BxPc-3, SW1990, PaCa-2 and Capan-2. Antisense **RAGE** suppressed the expression of matrix metalloproteinase 2 (MMP2) and MMP9 in those cells. Antisense **RAGE** suppressed cell invasion and cell adhesion to laminin-coating plate in those cells. **RAGE** participated in metastasis and invasion of human pancreatic tumor.

L4 ANSWER 8 OF 64 MEDLINE

AN 2002611052 MEDLINE

TI Receptor for advanced glycation end products (**RAGE**) signaling induces CREB-dependent chromogranin expression during neuronal differentiation.

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Oct 11) 277 (41) 38635-46.

Journal code: 2985121R. ISSN: 0021-9258.

AU Huttunen Henri J; Kuja-Panula Juha; Rauvala Heikki

AB Receptor for advanced glycation end products (**RAGE**) mediates neurite outgrowth and cell migration upon stimulation with its ligand, **amphoterin**. We show here that **RAGE**-dependent changes in cell morphology are associated with proliferation arrest and changes in gene expression in neuroblastoma cells. Chromogranin B, a component of secretory vesicles in endocrine cells and neurons, was found to be up-regulated by **RAGE** signaling during differentiation of neuroblastoma cells along with the two other members of the chromogranin family, chromogranin A and secretogranin II. Ligation of **RAGE** by **amphoterin** lead to rapid phosphorylation and nuclear localization of cyclic AMP response element-binding protein (CREB), a major regulator of chromogranin expression. Furthermore, inhibition of ERK1/2-Rsk2-dependent CREB phosphorylation efficiently inhibited up-regulation of chromogranin gene expression upon **RAGE** activation. To further study the effects of **RAGE** and **amphoterin** on cellular differentiation, we stimulated embryonic stem cells expressing **RAGE** or a signaling-deficient mutant of **RAGE** with **amphoterin**. **Amphoterin** was found to promote **RAGE**-dependent neuronal differentiation of embryonic stem cells characterized by up-regulation of neuronal markers light neurofilament protein and beta-III-tubulin, activation of CREB, and increased expression of chromogranins A and B. These data suggest that **RAGE** signaling is capable of driving neuronal differentiation involving CREB activation and induction of chromogranin expression.

L4 ANSWER 9 OF 64 CAPLUS COPYRIGHT 2003 ACS  
AN 2001:724797 CAPLUS  
DN 136:18922  
TI The multiligand receptor **RAGE** as a progression factor amplifying  
immune and inflammatory responses  
SO Journal of Clinical Investigation (2001), 108(7), 949-955  
CODEN: JCINAO; ISSN: 0021-9738  
AU Schmidt, Ann Marie; Yan, Shi Du; Yan, Shi Fang; Stern, David M.  
AB A review discussing the diverse functions of the multi-ligand receptor  
**RAGE**. It discusses the involvement of **RAGE** in diabetes,  
cellular dysfunction in the amyloidoses, propagation of the  
immune/inflammatory response, and in function of **amphotericin**.

(FILE 'HOME' ENTERED AT 16:40:54 ON 27 MAR 2003)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED  
AT 16:41:02 ON 27 MAR 2003

L1 3464 S (RECEPTOR FOR ADVANCED GLYCATION ENDPRODUCT?) OR RAGE  
L2 137 S L1 AND (LAMININ OR FIBRONECTIN OR AMPHOTERIN OR CADHERIN OR IN  
L3 64 DUP REM L2 (73 DUPLICATES REMOVED)  
L4 64 FOCUS L3 1-  
L5 14 S L4 AND PY<=1998  
L6 14 SORT L5 PY

=> d an ti so au ab pi l4 1

L4 ANSWER 1 OF 64 CAPLUS COPYRIGHT 2003 ACS

AN 1999:691229 CAPLUS

DN 131:317761

TI Inhibition of tumor invasion or spreading based on a soluble receptor for  
advanced glycation endproducts

SO PCT Int. Appl., 88 pp.

CODEN: PIXXD2

IN Schmidt, Ann Marie; Stern, David

AB The present invention provides for a method for inhibiting tumor invasion  
or metastasis in a subject which comprises administering to the subject a  
therapeutically effective amt. of a form of sol. receptor for advanced  
glycation endproducts (RAGE). Interruption of cellular  
RAGE-extracellular matrix (amphotericin and/or similar  
structures) interaction appears to be at least one mechanism by which  
sRAGE limits tumor growth. The present invention also provides a method  
for evaluating the ability of an agent to inhibit tumor invasion in a  
local cellular environment which comprises: (a) admixing with cell culture  
media an effective amt. of the agent; (b) contacting a tumor cell in cell  
culture with the media from step (a); (c) detg. the amt. of spreading of  
the tumor cell culture, and (d) comparing the amt. of spreading of the  
tumor cell culture detd. in step (c) with the amt. detd. in the absence of  
the agent, thus evaluating the ability of the agent to inhibit tumor  
invasion in the local cellular environment. The present invention also  
provides a pharmaceutical compn. which comprises a therapeutically  
effective amt. of the agent evaluated in the aforementioned method and a  
pharmaceutically acceptable carrier.

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|--|------|----------|-----------------|----------|
| WO 9954485   | A1   | 19991028 | WO 1999-US8427  | 19990416 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,<br>DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,<br>JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,<br>MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,<br>TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,<br>MD, RU, TJ, TM |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,<br>ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,<br>CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |      |          |                 |          |
| US 6465422   | B1   | 20021015 | US 1998-62365   | 19980417 |
| CA 2325573   | AA   | 19991028 | CA 1999-2325573 | 19990416 |
| AU 9934957   | A1   | 19991108 | AU 1999-34957   | 19990416 |
| EP 1071794   | A1   | 20010131 | EP 1999-916699  | 19990416 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,<br>IE, FI   |      |          |                 |          |
| JP 2002512038  | T2   | 20020423 | JP 2000-544814  | 19990416 |
| US 2002177550  | A1   | 20021128 | US 2001-851071  | 20010508 |

10 ANSWER 1 OF 69 CAPLUS COPYRIGHT 2003 ACS  
 AN 1996:748350 CAPLUS  
 DN 126:17792  
 TI Kidney carcinoma **tumor** rejection antigen **RAGE** TRA cDNA sequences, antigen recombinant production, and **cancer** diagnosis and treatment  
 SO PCT Int. Appl., 105 pp.  
 CODEN: PIXXD2  
 IN Gaugler, Beatrice; Van Den Eynde, Benoit; Schrier, Peter; Brouwenstijn, Nathalie; Boon-Falleur, Thierry  
 AB The invention describes the **RAGE tumor** rejection antigen precursor family, including nucleic acids encoding such **tumor** rejection antigen precursors, **tumor** rejection antigen peptides or precursors thereof and antibodies relating thereto. Methods and products also are provided for diagnosing and treating conditions characterized by expression of a **RAGE tumor** rejection antigen precursor.

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE         |
|---|------|----------|-----------------|--------------|
| PI WO 9629409   | A2   | 19960926 | WO 1996-US4037  | 19960321 <-- |
| WO 9629409  | A3   | 19961107 |                 |              |
| W: AU, CA, CN, JP, NO, NZ   |      |          |                 |              |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE    |      |          |                 |              |
| US 5939526  | A    | 19990817 | US 1995-530569  | 19950920     |
| AU 9654298  | A1   | 19961008 | AU 1996-54298   | 19960321 <-- |
| AU 705768   | B2   | 19990603 |                 |              |
| EP 815229   | A2   | 19980107 | EP 1996-911399  | 19960321 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI |      |          |                 |              |
| JP 11506904   | T2   | 19990622 | JP 1996-528658  | 19960321     |

L10 ANSWER 2 OF 69 CAPLUS COPYRIGHT 2003 ACS  
 AN 1999:518306 CAPLUS  
 DN 131:169277  
 TI Isolated **RAGE-1** derived peptides which complex with HLA-B7 molecules and uses thereof  
 SO U.S., 32 pp., Cont.-in-part of U.S. Ser. No. 408,015.  
 CODEN: USXXAM  
 IN Gaugler, Beatrice; Vanden, Eynde Benoit; Schrier, Peter; Brouwenstijn, Nathalie; Boon-Falleur, Thierry  
 AB The invention describes the **RAGE tumor** rejection antigen precursor family, including nucleic acids encoding such **tumor** rejection antigen precursors, **tumor** rejection antigen peptides or precursors thereof and antibodies relating thereto. Methods and products also are provided for diagnosing and treating conditions characterized by expression of a **RAGE tumor** rejection antigen precursor.

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE         |
|---|------|----------|-----------------|--------------|
| PI US 5939526   | A    | 19990817 | US 1995-530569  | 19950920     |
| ZA 9602280  | A    | 19960828 | ZA 1996-2280    | 19960320 <-- |
| CA 2211448  | AA   | 19960926 | CA 1996-2211448 | 19960321 <-- |
| WO 9629409  | A2   | 19960926 | WO 1996-US4037  | 19960321 <-- |
| WO 9629409  | A3   | 19961107 |                 |              |
| W: AU, CA, CN, JP, NO, NZ   |      |          |                 |              |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE    |      |          |                 |              |
| AU 9654298  | A1   | 19961008 | AU 1996-54298   | 19960321 <-- |
| AU 705768   | B2   | 19990603 |                 |              |
| EP 815229   | A2   | 19980107 | EP 1996-911399  | 19960321 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI |      |          |                 |              |
| CN 1179180  | A    | 19980415 | CN 1996-192650  | 19960321 <-- |
| JP 11506904   | T2   | 19990622 | JP 1996-528658  | 19960321     |

L15 ANSWER 4 OF 1211 CAPLUS COPYRIGHT 2003 ACS  
 AN 1988:527128 CAPLUS  
 DN 109:127128  
 TI **Tumor** necrosis factor **inhibits** collagen and **fibronectin** synthesis in human dermal fibroblasts  
 SO FEBS Letters (1988), 236(1), 47-52  
 CODEN: FEBLAL; ISSN: 0014-5793  
 AU Mauviel, A.; Daireaux, M.; Redini, F.; Galera, P.; Loyau, G.; Pujol, J. P.  
 AB **Tumor** necrosis factor (TNF) caused **inhibition** of collagen prodn. by confluent **cultures** of human dermal fibroblasts in a dose-dependent manner. Concomitant increase of prostaglandin E2 release was obsd. as a result of TNF-induced cell activation. However, a blockade of the cyclooxygenase pathway of arachidonate metab. by indomethacin did not abrogate the **inhibitory** effect of TNF on collagen synthesis, suggesting that this effect could be independent of prostaglandin metab. Gel electrophoresis of the newly synthesized macromols. from the **culture** media showed that both type I and type III collagens as well as **fibronectin** were affected by the **inhibition**. Electrophoresis of cell layer-assocd. proteins demonstrated that the redn. in amts. of collagen and **fibronectin** in the medium did not result from an intracellular accumulation of these macromols. Prodn. of procollagens was reduced in parallel to that of collagens, suggesting that the effect of TNF is exerted before the processing steps of procollagens. Thus, TNF could play a role in modulation of matrix deposition by fibroblasts during inflammatory processes.

L15 ANSWER 5 OF 1211 CAPLUS COPYRIGHT 2003 ACS  
 AN 1987:475396 CAPLUS  
 DN 107:75396  
 TI **Laminin** stimulates the attachment, spread and incorporation of 3H-TdR into **cancer** cells  
 SO Shengwu Huaxue Zazhi (1987), 3(3), 261-9  
 CODEN: SHZAE4; ISSN: 1000-8543  
 AU Zhou, Rouli; Gao, Suying; Wang, Su; Ma, Kangtao; Wang, Xinmin; Sun, Quan; Jing, Yueying; Zhang, Sha; Liang, Limin; Lin, Min  
 AB The attachment to basement membranes and the proliferation on defined matrixes of **cancer** cells are of fundamental importance in the processes of invasion and metastasis. The effects of **laminin** on **cancer** cell attachment, spread, and [3H]TdR incorporation was studied. The attachment of cells was quantitated by measuring LDH activity. **Laminin** markedly stimulated the attachment and spread of mouse S180-V sarcoma cells and B16-MBK melanoma cells in **culture** on solid support. **Fibronectin**, but not other glycoproteins such as egg albumin, showed similar stimulation of **cancer** cell attachment. Furthermore, cell attachment to **laminin** or **fibronectin** was specifically **inhibited** by antibody against **laminin** or **fibronectin**, resp. These results indicate that the role of **laminin** was specific. The surface of attached cells was obsd. under scanning electron microscope. **Cancer** cells attached to the surface of bare glass were round with numerous ruffles and microvilli. In contrast, those attached to the **laminin**-coated glass surface appeared polygonal and flat in morphol., with fewer ruffles and microvilli. In addn., the incorporation of [3H]TdR into **cancer** cells attached to **laminin** matrixes was substantially increased. The role of **laminin** in the invasion and metastasis of **cancer** cells is discussed.

(FILE 'HOME' ENTERED AT 16:40:54 ON 27 MAR 2003)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED  
AT 16:41:02 ON 27 MAR 2003

L1 3464 S (RECEPTOR FOR ADVANCED GLYCATION ENDPRODUCT?) OR RAGE  
L2 137 S L1 AND (LAMININ OR FIBRONECTIN OR AMPHOTERIN OR CADERIN OR IN  
L3 64 DUP REM L2 (73 DUPLICATES REMOVED)  
L4 64 FOCUS L3 1-  
L5 14 S L4 AND PY<=1998  
L6 14 SORT L5 PY  
L7 333 S L1 AND (CANCER OR TUMOR OR NEOPLAS? TUMOUR)  
L8 180 DUP REM L7 (153 DUPLICATES REMOVED)  
L9 69 S L8 AND PY<=1998  
L10 69 FOCUS L9 1-  
L11 33209 S (CANCER OR TUMOR OR NEOPLAS? OR TUMOUR) (L) (LAMININ OR FIBRO  
L12 10728 S L11 AND INHIBIT?  
L13 2282 S L12 AND (CULTURE OR IN(W)VITRO)  
L14 1211 S L13 AND PY<=1997  
L15 1211 FOCUS L14 1-  
L16 63 S (CANCER OR TUMOR OR NEOPLAS? OR TUMOUR) (L) AMPHOTERIN  
L17 28 DUP REM L16 (35 DUPLICATES REMOVED)  
L18 28 SORT L17 PY  
L19 4 S L18 AND PY<=1998

=> d an ti so au ab pi l19 1-4

L19 ANSWER 1 OF 4 MEDLINE  
AN 97433100 MEDLINE  
TI Differential messenger RNA and protein expression of the receptor for  
advanced glycosylated end products in normal lung and non-small cell lung  
carcinoma.  
SO CANCER RESEARCH, (1997 Sep 1) 57 (17) 3669-71.  
Journal code: 2984705R. ISSN: 0008-5472.  
AU Schraml P; Bendik I; Ludwig C U  
AB The receptor for advanced glycosylated end products (RAGE), a member of  
the immunoglobulin superfamily, was one of the cDNA subtraction clones  
that was found to be differentially expressed in human lung and the  
corresponding **tumor** tissue. In nine additional matched normal/  
**tumor** pairs, a strongly reduced or missing expression, not only on  
a transcriptional level but also on a protein level, was demonstrated in  
the non-small cell lung carcinoma tissue. Because **amphoterin**, a  
physiological ligand of RAGE that is highly expressed in the lung,  
mediates cell differentiation via RAGE, a down-regulation of the receptor  
may be considered as a critical step in lung **tumor** formation.  
Furthermore, we determined the complete reading frame of RAGE.

(FILE 'HOME' ENTERED AT 16:40:54 ON 27 MAR 2003)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED  
AT 16:41:02 ON 27 MAR 2003

L1 3464 S (RECEPTOR FOR ADVANCED GLYCATION ENDPRODUCT?) OR RAGE  
L2 137 S L1 AND (LAMININ OR FIBRONECTIN OR AMPHOTERIN OR CADERIN OR IN  
L3 64 DUP REM L2 (73 DUPLICATES REMOVED)  
L4 64 FOCUS L3 1-  
L5 14 S L4 AND PY<=1998  
L6 14 SORT L5 PY  
L7 333 S L1 AND (CANCER OR TUMOR OR NEOPLAS? TUMOUR)  
L8 180 DUP REM L7 (153 DUPLICATES REMOVED)  
L9 69 S L8 AND PY<=1998  
L10 69 FOCUS L9 1-  
L11 33209 S (CANCER OR TUMOR OR NEOPLAS? OR TUMOUR) (L) (LAMININ OR FIBRO  
L12 10728 S L11 AND INHIBIT?  
L13 2282 S L12 AND (CULTURE OR IN(W)VITRO)  
L14 1211 S L13 AND PY<=1997  
L15 1211 FOCUS L14 1-  
L16 63 S (CANCER OR TUMOR OR NEOPLAS? OR TUMOUR) (L) AMPHOTERIN  
L17 28 DUP REM L16 (35 DUPLICATES REMOVED)  
L18 28 SORT L17 PY  
L19 4 S L18 AND PY<=1998  
L20 115 S L1 AND AMPHOTERIN  
L21 48 DUP REM L20 (67 DUPLICATES REMOVED)  
L22 9 S L21 AND PY<=1998  
L23 9 SORT L22 PY

=> d an ti so au ab pi l23 1-9

L23 ANSWER 1 OF 9 MEDLINE

AN 96029671 MEDLINE

TI The receptor for advanced glycation end products (RAGE) is a cellular binding site for amphotericin. Mediation of neurite outgrowth and co-expression of rage and amphotericin in the developing nervous system.

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Oct 27) 270 (43) 25752-61.

Journal code: 2985121R. ISSN: 0021-9258.

AU Hori O; Brett J; Slaterry T; Cao R; Zhang J; Chen J X; Nagashima M; Lundh E R; Vijay S; Nitecki D; +

AB The receptor for advanced glycation end products (RAGE), a newly-identified member of the immunoglobulin superfamily, mediates interactions of advanced glycation end product (AGE)-modified proteins with endothelium and other cell types. Survey of normal tissues demonstrated RAGE expression in situations in which accumulation of AGEs would be unexpected, leading to the hypothesis that under physiologic circumstances, RAGE might mediate interaction with ligands distinct from AGEs. Sequential chromatography of bovine lung extract identified polypeptides with M(r) values of approximately 12,000 (p12) and approximately 23,000 (p23) which bound RAGE. NH2-terminal and internal protein sequence data for p23 matched that reported previously for amphotericin. Amphotericin purified from rat brain or recombinant rat amphotericin bound to purified sRAGE in a saturable and dose-dependent manner, blocked by anti-RAGE IgG or a soluble form of RAGE (sRAGE). Cultured embryonic rat neurons, which express RAGE, displayed dose-dependent binding of 125I-amphotericin which was prevented by blockade of RAGE using antibody to the receptor or excess soluble receptor (sRAGE). A functional correlate of RAGE-amphotericin interaction was inhibition by anti-RAGE F(ab')2 and sRAGE of neurite formation by cortical neurons specifically on amphotericin-coated substrates. Consistent with a potential role for RAGE-amphotericin interaction in development, amphotericin and RAGE mRNA/antigen were co-localized in developing rat brain. These data indicate that RAGE has physiologically relevant ligands distinct from AGEs which are likely, via their interaction with the receptor, to participate in physiologic processes outside of the context of diabetes and accumulation of AGEs.

L23 ANSWER 2 OF 9 SCISEARCH COPYRIGHT 2003 ISI (R)  
 AN 95:201535 SCISEARCH  
 TI THE RECEPTOR FOR ADVANCED GLYCATION ENDPRODUCTS (**RAGE**) IS A  
 CELL-SURFACE RECEPTOR FOR **AMPHOTERIN** IN THE DEVELOPING  
 CENTRAL-NERVOUS-SYSTEM (CNS) TO PROMOTE NEURITE OUTGROWTH  
 SO FASEB JOURNAL, (09 MAR 1995) Vol. 9, No. 3, Part 1, pp. A382.  
 ISSN: 0892-6638.  
 AU HORI O (Reprint); CAO R; BRETT J; SLATTERY T; NAGASHIMA M; NITECKI D;  
 MORSER J; STERN D; SCHMIDT A M

L23 ANSWER 3 OF 9 MEDLINE  
 AN 97433100 MEDLINE  
 TI Differential messenger RNA and protein expression of the receptor for  
 advanced glycosylated end products in normal lung and non-small cell lung  
 carcinoma.  
 SO CANCER RESEARCH, (1997 Sep 1) 57 (17) 3669-71.  
 Journal code: 2984705R. ISSN: 0008-5472.  
 AU Schraml P; Bendik I; Ludwig C U  
 AB The receptor for advanced glycosylated end products (**RAGE**), a  
 member of the immunoglobulin superfamily, was one of the cDNA subtraction  
 clones that was found to be differentially expressed in human lung and the  
 corresponding tumor tissue. In nine additional matched normal/tumor pairs,  
 a strongly reduced or missing expression, not only on a transcriptional  
 level but also on a protein level, was demonstrated in the non-small cell  
 lung carcinoma tissue. Because **amphoterin**, a physiological  
 ligand of **RAGE** that is highly expressed in the lung, mediates  
 cell differentiation via **RAGE**, a down-regulation of the receptor  
 may be considered as a critical step in lung tumor formation. Furthermore,  
 we determined the complete reading frame of **RAGE**.

L23 ANSWER 4 OF 9 MEDLINE  
 AN 97184302 MEDLINE  
 TI The receptor for advanced glycation end products mediates the chemotaxis  
 of rabbit smooth muscle cells.  
 SO DIABETES, (1997 Mar) 46 (3) 463-72.  
 Journal code: 0372763. ISSN: 0012-1797.  
 AU Higashi T; Sano H; Saishoji T; Ikeda K; Jinnouchi Y; Kanzaki T; Morisaki  
 N; Rauvala H; Shichiri M; Horiuchi S  
 AB Long-term incubation of proteins with glucose leads to advanced glycation  
 end products (AGEs) with fluorescence and a brown color. We recently  
 demonstrated immunologically the intracellular AGE accumulation in smooth  
 muscle cell (SMC)-derived foam cells in advanced atherosclerotic lesions.  
 To understand the mechanism of AGE accumulation in these foam cells, we  
 have now characterized the interaction of AGE proteins with  
 rabbit-cultured arterial SMCs. In experiments at 4 degrees C, 125I-labeled  
 AGE-bovine serum albumin (AGE-BSA) showed a dose-dependent saturable  
 binding to SMCs with an apparent dissociation constant (Kd) of 4.0  
 microg/ml. In experiments at 37 degrees C, AGE-BSA underwent  
 receptor-mediated endocytosis and subsequent lysosomal degradation. The  
 endocytic uptake of 125I-AGE-BSA was effectively inhibited by unlabeled  
 AGE proteins such as AGE-BSA and AGE-hemoglobin, but not by acetylated LDL  
 and oxidized LDL, well-known ligands for the macrophage scavenger receptor  
 (MSR). Moreover, the binding of 125I-AGE-BSA to SMCs was affected neither  
 by **amphoterin**, a ligand for one type of the AGE receptor, named  
**RAGE**, nor by 2-(2-furoyl)-4(5)-(2-furanyl)-1H-imidazole-hexanoic  
 acid-BSA, a ligand for the other AGE receptors, p60 and p90. This  
 indicates that the endocytic uptake of AGE proteins by SMCs is mediated by  
 an AGE receptor distinct from MSR, **RAGE**, p60, and p90. To  
 examine the functional role of this AGE receptor, the migratory effects of  
 AGE-BSA on these SMCs were tested. Incubation with 1-50 microg/ml of  
 AGE-BSA for 14 h resulted in significant dose-dependent cell migration.  
 The AGE-BSA-induced SMC migration was chemotactic in nature and was  
 significantly inhibited (approximately 80%) by an antibody against  
 transforming growth factor-beta (TGF-beta), and the amount of TGF-beta  
 secreted into the culture medium from SMC by AGE-BSA was sevenfold higher  
 than that of control, indicating that TGF-beta is involved in the  
 AGE-induced SMC chemotaxis. These data suggest that AGE may play a role in  
 SMC migration in advanced atherosclerotic lesions.

L23 ANSWER 5 OF 9 MEDLINE



AN 1999030344 MEDLINE  
 TI Sp1-binding elements in the promoter of **RAGE** are essential for  
**amphotericin**-mediated gene expression in cultured neuroblastoma  
 cells.  
 SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Nov 20) 273 (47) 30870-8.  
 Journal code: 2985121R. ISSN: 0021-9258.  
 AU Li J; Qu X; Schmidt A M  
 AB Receptor for AGE (**RAGE**) and the polypeptide **amphotericin**  
 are highly expressed and co-localized in neurons of the developing central  
 nervous system of the rat. In vitro, the interaction of **amphotericin**  
 with neuronal **RAGE** induces neurite outgrowth. We tested the  
 hypothesis that interaction of **amphotericin** with neuronal cells  
 enhances **RAGE** expression, thereby providing a mechanism by which  
**amphotericin**-mediated regulation of **RAGE** might contribute  
 to promotion of neurite growth and spreading. Incubation of cultured  
 neuroblastoma cells with **amphotericin** resulted in increased  
 transcription and translation of **RAGE**, a process largely  
 inhibited in the presence of anti-**RAGE** IgG but not by nonimmune  
 IgG. To begin to delineate molecular mechanisms underlying these findings,  
 we identified multiple putative binding elements within the 5'-flanking  
 region of the **RAGE** gene for Sp1, a transcription factor that has  
 been critically linked to the process of normal development. DNase I  
 footprinting and electrophoretic mobility shift assays demonstrated  
 multiple functional Sp1-binding sites within the region -245 to -40 of the  
**RAGE** promoter. Transient transfection of cultured SK-N-SH  
 neuroblastoma cells with chimeric 5'-deletion constructs linked to  
 luciferase reporter revealed that the region containing Sp1-binding  
 elements did not contribute uniquely to basal expression of the  
**RAGE** gene. Simultaneous mutation of the multiple Sp1-binding  
 elements in this region did not affect basal promoter function; however,  
 promoter responsiveness to **amphotericin** was markedly attenuated.  
 These results point to Sp1-dependent mechanisms underlying  
**amphotericin**-mediated increases in **RAGE** expression in  
 neuroblastoma cells and further link **amphotericin-RAGE**  
 interaction to development of the nervous system.